

Meiss is directed to a wound covering having connected discrete elements. The wound covering described is formed from a permeable web comprising ceramic or glass at least at the surface. The covering has either a plurality of individual elements either made or coated with ceramic or glass and connected by means of connecting members into a network or a permeable base web provided with a layer of ceramic or glass. The elements can be made of a bioinert material or bioactive material such as a calcium phosphate, preferably tricalcium phosphate, or hydroxy apatite. The elements may also be formed of bioglass or bioglass ceramic materials. Meiss distinguishes this wound covering from those of the prior art as the opposite of previously known surgical dressings which utilized ceramic microparticles. *See column 1, lines 44-68.* Rather, Meiss teaches a phalanx of discrete pieces of bioactive glass in various geometric shapes physically connected to form a protective cover for the injured area.

Low et al. is directed to a method and composition for repair of periodontal osseous defects based on particulate bioactive and biocompatible glass. According to the detailed description of the invention, the previously used synthetic materials produced mixtures that were not cohesive. These synthetic materials included tricalcium phosphate and hydroxyapatite. Low et al., rather, teach the use of bioactive glass powders of certain compositions and of a specific range of sizes, specific surface areas, specific pore distributions and specific surface chemistry. *See column 4, lines 24-28.*

Coleman et al. describe mandibular reconstruction with composite microvascular tissue transfer. Wood describes the case study of a man whose leg wound was treated by use of a sodium chloride impregnated dressing.

According to the Office Action, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to modify the Meiss wound covering product to allow release of ions, per Wood, into the wound, per Low et al., which shows ion migration from the glass upon bonding to a bone wound. Moreover, the Action states that a person of ordinary skill in the art would have been motivated to make this

modification for the purpose of ion release into a wound, for the advantages taught by Wood. Applicants respectfully disagree.

First, Meiss and Low et al. teach solutions to very different problems. Meiss is directed to a wound covering which obviates the problems with prior art wound coverings which did not have suitable oxygen and liquid permeability, tissue-compatibility and mechanical flexibility. Meiss had determined that the microparticles previously used did not provide each of these properties. The solution discovered by Meiss was the use of a mat, web or fabric comprising a plurality of individual elements, each having a surface of ceramic or glass. Low et al., on the other hand, is directed to the repair of periodontal osseous defects. The desired properties for such a material would not include suitable oxygen and liquid permeability or mechanical flexibility. Low et al. wanted to form a cohesive mass which could be placed in the periodontal defect where it stays in place despite suction or irrigation. Low et al. discovered specific glass powders which form such a cohesive mass and are easily manipulated for the purpose of packing densely into a periodontal defect for bonding to the bone.

In view of the completely different problems being solved by Meiss and Low et al., there would not have been any motivation by one of ordinary skill in the art to combine these references in any way.

Moreover, such a combination would not result in the presently claimed invention. The webs of Meiss would not function as intended if the layer of bioactive glass were replaced with the particles described in Low et al. As noted above, Meiss distinguished his webs from the prior art compositions used to treat wounds which included ceramic microparticles. Meiss, rather, indicated that the prior art particulate compositions did not provide suitable mechanical flexibility. Accordingly, Meiss teaches away from the use of particulate matter as taught by Low et al., thus teaching away from the combination of references proposed by the Examiner.

Low et al. also teaches away from the combination suggested by the Examiner. Low et al. specifically provides information regarding the poor results obtained when materials taught by Meiss, such as tricalcium phosphate, or hydroxy apatite, are used. Moreover, the compositions in Low et al. would not be effective for bone repair if they were replaced with the web structures of Meiss since Low et al. go into explicit detail about the requirements for their particulate composition. In particular, the compositions must not only be particulate, but must be of a particular range of particle sizes or the compositions would be inadequate. *See column 7, line 48 - column 8, line 61.*

In view of the particular teachings of both Meiss and Low et al., the combination of these patents is improper. Both references *teach away* from such a combination.

The addition of Coleman et al. and Wood do not remedy this deficiency of Meiss and Low et al. since neither of those documents provides the missing motivation to combine the primary references. Each is directed to a discussion of particular results in particular cases. According to the Examiner, Wood would teach the combination of Meiss and Low et al. to allow release of ions into the wound. Applicants disagree. Meiss teaches that use of particulates does not provide the needed qualities of a wound covering. Thus, one of ordinary skill in the art would not combine Meiss and Low et al. even given the teachings of Wood.

Even if the cited art were combined as described by the Examiner, the claimed invention would not have been obvious to one of ordinary skill in the art from such a combination.

The whole point of Meiss is to provide a web structure of interconnected elements. The claimed invention, however, provides for non-interlinked particles which are intended to react with tissue to develop extremely high surface areas, which is not possible with interconnected particles. Further, the particles are intended to be mixed with antibiotic to form a composition. While an interlinked glass composition can be combined with an antibiotic, it cannot be mixed in the same way as small, non-interlinked particles can be.

Moreover, as noted in Examples 1 and 2 of the present application, by mixing bioactive glass and an antibiotic, and placing the mixture into a wound, the healing time of wounds is substantially reduced. The bioactive glass, because it is non-interlinked, penetrates into the wound in a manner which is not possible with an interlinked mesh or web. Neither of Meiss or Low et al. provide this advantage and a combination of their teachings would not result in such a wound dressing structure. In view thereof, Applicants request that the Examiner withdraw the rejection under 35 U.S.C. § 103.

Claims 19-20 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Meiss, U.S.P. No. 5,000,746, in view of Low et al., U.S.P. No. 4,851,046, Coleman et al., and Wood, and further in view of Theilemann and Freed. This rejection under 35 U.S.C. § 103 is respectfully traversed.

Theilemann is directed to a two-layer bandage made of a polymer and a water-absorbing material. The polymer layer is permeable to gas and vapor and impermeable to water. The second layer is made of cellulose or wadding and is saturated with water or with an aqueous solution such as of an antibiotic. Freed discloses the use of injectable biomaterials for the repair of structurally defective or inadequately functioning muscles of the anal sphincter. Preferred biomaterials are collagen formulations.

According to the Office Action, it would have been *prima facie* obvious to modify the wound dressings of Meiss and Low et al. to include a carrier. Applicants respectfully disagree. As discussed above, Meiss and Low et al. are directed to solving completely different problems. Moreover, the teachings of the solutions to those problems are such that each patent teaches away from a combination with the teachings of the other. Thus, the combination of Meiss and Low et al. is improper. The teachings of Theilemann and Freed do not remedy this deficiency. In view thereof, a *prima facie* case has not been made and Applicants respectfully request that this rejection be withdrawn.

Claims 22-23 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Meiss, U.S.P. No. 5,000,746, in view of Low et al., U.S.P. No. 4,851,046, Coleman et al., and Wood, and further in view of Loeffler et al. The rejection under 35 U.S.C. § 103 is respectfully traversed.

Loeffler et al. relates to a kit for *in situ* formation of a topical gel for enzyme release in wounds. The kit includes a container for the active agent, a container for a solvent for the active agent and the chamber of an applicator containing a gelation agent, arranged so that the contents of the three containers can be rapidly mixed.

As discussed above, the combination of Meiss and Low et al. would not have made the claimed invention obvious to one of ordinary skill in the art since each patent teaches away from use of the materials as taught by the other patent. The addition of Loeffler et al. does not provide the requisite motivation for such a combination. Therefore, Applicants respectfully request that this rejection be withdrawn.

Applicants believe they have responded to all matters raised in the above referenced Office Action and that the application is now in condition for allowance. If the Examiner has any questions concerning this Application or this Reply and Amendment, he is invited to contact the undersigned.

Respectfully submitted,

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